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*Editorial Comment*

# The ERA-EDTA Working Group on inherited kidney disorders

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## Why a Working Group on inherited kidney disorders?

Dozens of inherited diseases affect the kidney; collectively, they account for at least 10% of patients with end-stage renal disease in Europe [1]. The underlying genetic defects may affect all structures and cell types of the nephron and may therefore compromise all aspects of kidney function. In addition, extra-renal involvement is frequently associated. In terms of frequency, inherited kidney disorders vary from relatively frequent diseases, such as autosomal dominant polycystic kidney disease (ADPKD, that arguably affects one in every 1000 person), to 'rare' diseases that, by definition, affect less than five persons in every 10 000.

Inherited kidney diseases concern a large number of patients in Europe and have a negative impact on the quality of life of the patients, who are often children, and of family members and relatives [2–5]. Most of these diseases are chronically debilitating conditions; some are life threatening. Low incidence, frequent phenotypic variability, lack of standardized diagnostic procedures and fragmentation of clinical and biological data (obtained mostly from small cohorts) limit our knowledge of many inherited disorders. These limitations include not only the underlying molecular mechanism(s) of disease but also the natural course and the impact of the diseases on quality of life, hampering possibilities to perform clinical studies and hindering progress in diagnosis and treatment [6, 7]. Furthermore, the low prevalence of such disorders implies a lack of priority for the pharmaceutical industry. The uneven perception of the impact of these diseases on the health care burden is reflected by discrepancies in public and private funding schemes across European countries.

As physicians and nephrologists, we recognize the health care priority represented by inherited kidney diseases in the community and are committed to improving the medical treatment of affected individuals.

## Post-genomic era: need for exchange and international networks

The establishment of an unequivocal genetic diagnosis is essential to define the disease entity, to characterize the pathophysiology, to screen and stratify patients for observational and interventional studies, to predict disease course and outcomes and, ultimately, to improve care, follow-up and support. The past three decades have witnessed a revolution in molecular biology and genetics that has changed the way we understand monogenic diseases. More recently, these changes have also impacted our perception of more common multigenic disorders. It is now increasingly recognized that genetic factors also influence most aspects of renal function in the general population and represent important determinants for the progression of chronic renal failure in acquired kidney diseases [8–10]. Bioinformatics and

technical advances in the post-genome era, including rapid development of next-generation sequencing technologies (e.g. exome and whole-genome sequencing, with increasingly refined methods to filter the identified variants) have opened new perspectives for the diagnosis, screening and pre-symptomatic testing of Mendelian diseases. These advances are paralleled by more precise in-depth phenotyping of patients and by the increasing availability of model organisms, transgenic mice and cell culture systems which provide insights into the biological role of encoded proteins and their involvement in disease process. Altogether, these advances are crucial to improve diagnostic and follow-up tests, to design new target-based therapeutics and, potentially, to predict response to pharmacotherapy as well as adverse drug events [5, 11].

The clinical and research community at large is aware of the necessity to disseminate new scientific knowledge on rapid advances in technology for molecular diagnosis and on their consequences (including technical and ethical limitations) for the identification of single gene defects, complex diseases and disorders with oligogenic modes of inheritance [12, 13]. These efforts require exchange and networking between patients, patient caregivers, geneticists, clinicians, laboratory scientists and researchers from the pharmaceutical industry to develop translational approaches. The latter should involve complementary teams that are able to cover the spectrum of individual diseases in terms of clinical investigations, registries, molecular diagnosis and modelling/pathophysiology [4, 5, 14]. Patient organizations should be involved in this effort from the start [15]; their contribution is essential, in particular in promoting public awareness and fostering research aimed at early diagnosis and improved treatment. In times of budgetary constraints, international networks are also crucial to avoid the fragmentation of knowledge and duplication of efforts.

Finally, with the identification of an increasing number of monogenic diseases, it has become evident that insights on inherited kidney diseases are also relevant for our fundamental knowledge of renal physiology/biochemistry and of more common clinical problems, such as renal disease progression, blood pressure control, kidney stone formation and multi-systemic involvement of renal diseases.

## Objectives of the Working Group

The creation of the ERA-EDTA Working Group on Inherited Kidney Disorders (WGIKD) aims at filling a gap in European nephrology and mobilizing a critical mass of expertise towards the following objectives:

- to encourage '*research*', on a Europe-wide scale, on the natural history and mechanisms of inherited diseases affecting the kidney. These disorders include orphan nephropathies affecting all components of the kidney and cystic kidney disorders;
- to address the need for '*epidemiology*' data and registries, the necessity for earlier and more efficient '*diagnosis*', the identification of new '*therapeutic targets*' and improved and affordable care;
- to facilitate the '*dissemination of knowledge*' to health care providers, patients and their families, patient support groups, health authorities and policymakers and industry;
- to organize '*dedicated meetings*', in conjunction with the annual ERA-EDTA congress and on specific occasions (focus on education, ethics, policies and research proposals).

Ultimately, disseminating knowledge, increasing awareness and promoting basic and clinical investigations should pave the way for a better global care of these disorders (Figure 1).

## Ongoing projects

The activities of the ERA-EDTA WGIKD include:

- a dedicated symposium during the annual ERA-EDTA Congress as well as during the European Society of Pediatric Nephrology;
- the elaboration and publication of 'best practice' guidelines on selected topics of wide interest, in collaboration with the relevant societies and the European Renal Best Practice group of the ERA-EDTA;

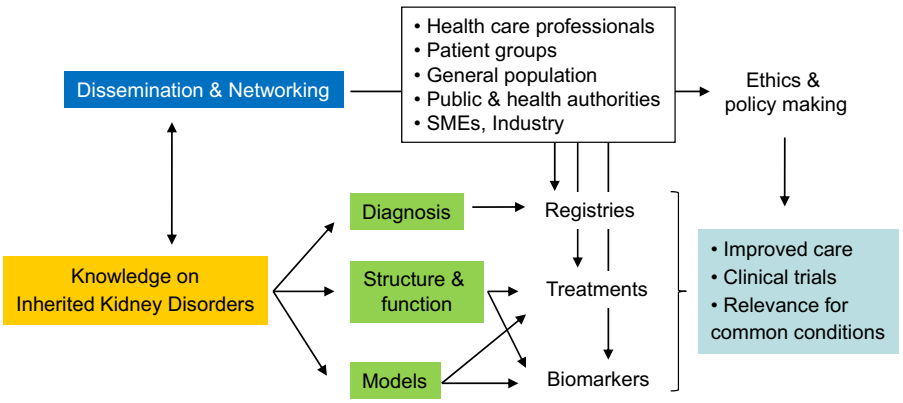


**Fig. 1.** Pathways of translating knowledge on inherited kidney disorders to clinical applications.

- the organization of continuous medical education seminars in various locations in Europe, targeting local needs;
- the support of research projects addressing critical issues related to inherited kidney diseases (e.g. the EuroCYST initiative to create a European cohort of patients with ADPKD);
- the support for registries, cohorts and recruitment of defined patient groups, and the diffusion of knowledge and support at a local level.

These activities, as well as specific announcements and relevant informations, will be posted regularly on the website (http://www.era-edta.org/wgikd/ERA-EDTA_working_group_on_Inherited_kidney_disorders.htm).

Active communication between the Working Group, organizations involved in strategic programmes on rare/inherited kidney diseases, patient support groups and adult and paediatric nephrology societies in Europe is ongoing.

## Membership

The establishment of the ERA-EDTA WGIKD offers the opportunity to gather individuals concerned by all types of inherited nephropathies, including ADPKD (which is usually not considered a rare disease by health policy makers) across Europe. The Working Group aims at fostering exchange between adult and paediatric nephrologists, clinicians and scientists across disciplines ranging from general internal medicine to urology and nephrology and genetics and more fundamental areas of science.

Core members of the Working Group are currently involved in several European Union (EU)-funded projects addressing kidney diseases (EuReGene, Genecure, EUNEFRON, PodoNet, ESCAPE and EuroCYST), in addition to national and international collaborative efforts in clinical and fundamental research in inherited kidney disorders. The body of expertise available in the network should facilitate a better coordination to diffuse scientific knowledge and raise public awareness for inherited nephropathies in the EU, in collaboration with patient associations and public institutions, within the context of policies developed by the ERA-EDTA. The initial phase of the network already involves >50 groups, totalizing 200+ participants from all across Europe.

Enrolment in the Working Group is free and easy through the ERA-EDTA website (see above) or by sending an email to wgikd@era-edta.org.

*Conflict of interest statement*. None declared.

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